Office Action Summary	Application No. 09/616,283	Applicant(s) GOODNOW, TIMOTHY T.	
	Examiner Ja-Na A Hines	Art Unit 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *14 July 2000* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Specification

1. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

2. The use of the trademark TRITON™ has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1, 7-9,12-14, 17-19, and 21-22 are vague and indefinite in the recitation of screening of a clinically relevant amount of bacteria. It is unclear how to define a clinically relevant amount. Neither the specification nor the claims teach how to define a clinically relevant amount. No requisite amounts for

determining clinical relevance are taught. Therefore, the term is vague and indefinite.

Claims 1, 7-9,12-14, 17-19, and 21-22 are unclear because the claims do not recite how to determine "binding of the set of binding agents to the sample." It is unclear how the binding agents bind sample. The claims state that the binding agents specifically bind to gram-negative or positive antigens and not to the sample. Therefore, the sample is unclear with respect to what the binding agents specifically bind to.

Again, the claims are unclear because the binding indicates the presence of clinically relevant bacteria. It is unclear without a detectable label to indicate binding of the complex, how can one of ordinary skill in the art determine presence of bacteria?

5. Claims 1-22 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: There is no contact step which contacts the binding agents with the gram-negative or positive antigen potentially found in the sample to indicate the presence of bacteria. There is no detection step that detects the binding complex and indicates the presence of the bacterial antigen.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1-2, 4, 6-8 and 14-22 are rejected under 35 U.S.C. 102(b) as being anticipated by Young (US Patent 5,698,198). Young (US Patent 5,698,198) teaches methods for treating gram-negative bacterial infections in humans. Bacterial sepsis and related septic shock are frequently lethal conditions caused by infections that can result from certain types of surgery and transplanation therapy or other disease states (col. 1 lines 27-30). Gram-negative bacteria endotoxins contain a common core structure and may contain individual capsule and surface polysaccharide (col. 2 lines 10-13). The core lipopolysaccharide (LPS) structure is widely shared among the diverse gram-negative bacterial genera and their endotoxins (col. 2 lines 10-15). The core structure is significant because it is associated with endotoxicity and because it is conserved in gram-negative bacteria (col. 2 lines 19-23). Antibodies or active fragments that bind with the core structure can have broad reactivity with a number of gram-negative bacteria (col. 2 lines 34-37). The present invention teaches monoclonal antibodies that bind to epitopes found on LPS most commonly associated with the endotoxin core and exhibit broad cross-reactivity with gram-negative bacteria (col. 4 lines 59-64). Also taught is a monoclonal antibody that binds to epitopes found on gram-positive bacteria (col.4 lines 65-66). Detection methods are well known in the art and include using

antibodies in enzyme-linked immunoassays (EIA) and immunodot assay (col. 6 lines 13-16). Antibody is bound to antigen for detection with a labeled antibody reactive with the anti-LPS antibody (col. 6 lines 20-22). Appropriate labels include radioisotopes, luminescent substrates such as fluorescing agents and components of enzymatic labels (col. 21-24). Monoclonal antibodies have been used with a diagnostic agents in *in vitro* test to test for the presence of gram negative bacteria or bacteria generally in mammals by subjecting body fluids of tissues or other human-derived substances or fluids to standard immunoassay protocols (col. 6 lines 52-56). Assays include formats where body fluid is contacted to antibodies of the present invention and a labeled second antibody used to detect the presence of bacteria to which the antibodies are bound (col. 6 lines 60-64). Alternatively, a competitive immunoassay or a "sandwich" type assay can be employed (col. 6 lines 64-66). Well known methods can be found in cited prior art incorporated by reference (col. 7 lines 1-3). Tables 9 and 10 teach the binding of a monoclonal antibody activity to LPS found in both gram negative and positive bacteria. See Example II B-2. Also taught are enzyme linked immunoassay using whole bacteria, see Example III B, and using purified LPS, see Example III C. Diagnostic EIA are taught in Example XIII where tissue extract from a patient is applied to a matrix with antibodies.

Inherently, Young teaches all the components of the kit, i.e., binding agent and a detection means. Young teaches the use of these components. Furthermore, to include well-known and available components in a kit to increase efficiency in the performance of the assay and for economical benefits is not found patentable.

Therefore, Young teaches a method for screening for the presence of an amount of bacteria in blood, blood products, or tissue fluids comprising the same steps as recited in the instant application.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 3 and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Young (US Patent 5,698,198) in view of Richards (US Patent 5,043,267). Young (US Patent 5,698,198) et al., has been discussed above, however Young does not teach a binding agent which specifically binds to the lipotechoic acid structure of gram-positive bacteria.

Richards (US Patent 5,043,267) teaches methods for rapid detection of bacterial infections. It is well known to detect gram-positive and negative bacteria (col. 3 lines 35-36). Bacteria belonging to these families are known to be phagocytosed by phagocytes which comprise polymorphonuclear leukocytes (PMN), monocytes and tissue macrophages (col. 3 lines 45-48). The instant invention teaches detection of partially degraded or phagocytosed bacteria (col. 3 lines 31-34). Cellular populations which are suitable for practice the method of detecting in blood, urine, spinal fluid, synovial fluid, mucosal secretion and scrapings, however PMN's are preferable (col. 3-4

lines 67-3). Antibody based systems for detection includes a variety of immunoassays, such as a radioimmunoassay, enzyme-linked immunosorbent assay, radial diffusion, complement fixation and a host of others (col. 4 lines 63-68). The invention teaches detection of a lipoteichoic acid, a component of *Streptococcus faecalis*. Example 2 teaches preparation of a monoclonal antibody using purified lipoteichoic acid (LTA) obtained from *Streptococcus faecalis* as the antigen (col. 7 lines 60-65). Gram-positive bacteria are known to possess LTA on or near the cell surface (col. 8 lines 103). Antibodies specific for the polyglycerolphosphate portion of LTA were selected based upon the binding ability (col. 8 lines 3-6). This selection provides monoclonal antibodies with a greater probability of reacting with the LTA (col. 8 lines 10-14). Immunoassays were performed using the antibody reagents (col. 8 lines 30-35).

Therefore no more than routine skill would have been required at the time of applicants invention to substitute the use of a well known binding agent which binds lipotechoic acid of gram-positive bacteria as taught by Richards in the method of screening for gram-negative and positive bacteria as taught by Young, because Richards teaches that monoclonal antibodies which bind to the lipotechoic acid of gram-positive can detect bacteria that ~~has~~ have been partially degraded, which is a form found in blood.

Prior Art

8. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Arduino et al., teach growth and endotoxin production of *Yersinia* and *Enterobacter* in erythrocytes. Connelly EP 279,517 teach sandwich assays

for detecting lipopolysaccharides of gram-negative bacteria using immobilized binding proteins and labeled detection reagents. Tadler et al., teach sandwich immunoassay for the detection of lipoteichoic acid found in gram-positive bacteria.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na A Hines whose telephone number is 703-305-0487. The examiner can normally be reached on Monday-Thursday and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 703-308-3909. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Ja-Na Hines
September 25, 2001

L. F. Smith
LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
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